*REMARKS/ARGUMENTS*

*The Present Invention*

The present invention is directed to a method of inhibiting the binding of a chaperone protein with its client protein or client polypeptide in a mammal which consists essentially of contacting a chaperone protein with a coumarin or coumarin derivative, wherein about 100 mg/kg of coumarin or coumarin derivative is administered to a mammal at least once per day for about 5 days and, wherein the chaperone protein is heat shock protein (Hsp) 90.

*The Pending Claims*

Claims 1 and 3-13 are currently pending.

*Amendments to the Claims*

Claims 14-17 have been canceled. Claim 1 has been amended to correctly spell the word "coumarin" at line 6 of this claim as pointed out by the Office.

*The Office Action*

Claims 1 and 3-17 have been objected to because of a misspelling of the term coumarin in claim 1. Claims 1 and 3-17 have been rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. Claims 1 and 3-17 have been rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. Claims 14-17 have been rejected for adding new matter. Claims 1, 3, and 5-15 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Eder et al. (Cancer Res., 49, 595-598 (1989)) as evidenced by Marcu et al. (*J. Biochem.*, 275:47, 37181-37186 (2000)). Claims 1, 16, and 17 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Civitico et al. (*J. Med. Vir.*, 31: 90-97 (1990)) as evidenced by Hu et al. (*PNAS*, 93: 1060-1064 (1996)). Claims 1, 3, and 4 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Eder et al., as evidenced by Marcu et al., in view of Gormley.

*Discussion of Rejections Under 35 U.S.C. § 112, second paragraph*

Claims 1 and 3-17 have been rejected as allegedly indefinite under 35 U.S.C. § 112, second paragraph. Claims 14-17 have been canceled, and accordingly, Applicants' response will be limited to claims 1 and 3-13. The Office acknowledges that the claimed method is limited to specified steps by Applicants use of the preamble transitional phrase "consisting essentially of," however, the Office contends that neither the claims nor the specification

provide a clear teaching of the novel characteristics that should be preserved with the claimed invention. Applicants traverse this rejection.

First, Applicants point out that independent claim 1, from which all other claims depend, recites a number of limitations clearly identifying the novel characteristics of the instant invention. Claim 1 recites a method of inhibiting binding of a chaperone protein with its client protein or client polypeptide in a mammal, wherein the method consists essentially of:

- contacting a chaperone protein with coumarin or a coumarin derivative, such that the coumarin or the coumarin derivative binds the chaperone protein, which binding inhibits the chaperone protein from binding its client protein or client polypeptide,
- wherein about 100 mg/kg of coumarin or coumarin derivative is administered to a mammal
- at least once per day
- for about 5 days and,
- wherein the chaperone protein is heat shock protein (Hsp) 90.

*(bullet points added for emphasis)*

Thus, claim 1 clearly defines the metes and bounds of Applicants' invention in a way that is readily understood by one skilled in the art.

Further, Applicants submit that the Office has improperly interpreted the transitional phrase "consisting essentially of" as "comprising." The phrase "consisting essentially of" is well understood in the Patent Law to signal that the invention must include the recited steps and is only open to un-recited steps that do not materially affect the basic and novel properties of the invention. *PPG Indus. V. Guardian Indus. Corp.*, 145 F.3d 1351 (Fed. Cir. 1998). For example, combining the instant inventive method with the administration of another compound capable of affecting chaperone protein interactions, materially affects Applicants' basic invention. A person having ordinary skill in the art would understand that the later combination materially differs from the metes and bounds of the claims. Accordingly, the claims as presented clearly define the inventive methods, and thus, Applicants respectfully request withdrawal of the rejection under Section 112, second paragraph.

*Discussion of Rejections Under 35 U.S.C. § 112, first paragraph*

Claims 1 and 3-17 have been rejected as failing to comply with the written description requirement under 35 U.S.C. § 112, first paragraph. Claims 14-17 have been canceled, and accordingly, Applicants' response will be limited to claims 1 and 3-13. The Office contends that the claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the Applicants had possession of the

claimed invention at the time the application was filed. The Office agrees that the specification describes a method of inhibiting binding of a chaperone protein with its client protein or client polypeptide in a mammal, wherein the method consists essentially of contacting a chaperone protein with coumarin or a coumarin derivative, such that the coumarin or the coumarin derivative binds the chaperone protein, which binding inhibits the chaperone protein from binding its client protein or client polypeptide, wherein 100 mg/kg of coumarin or coumarin derivative is administered to a mammal at least once per day for 5 days and, wherein the chaperone protein is heat shock protein (Hsp) 90. However, the Office contends that the use of the word "about" in the recitation of dosage and frequency of dosage (i.e. about 100 mg/kg and about 5 days) are outside the scope of what is supported by the specification. Applicants traverse this rejection.

The word "about" is supported by the specification, and does not alter the scope of the claims relative to the specification. First, the specification recites the word "about" at, for example, page 15, line 34 in describing the concentration of coumarin derivative, novobiocin, needed to inhibit binding of a chaperone protein with its client protein. Further, the term "about" has been held to be clear, but flexible, without materially altering the substance of the invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540 (Fed. Cir. 1983). Accordingly, Applicants have literally satisfied the written description requirement for use of the term "about" in the context of administering a coumarin or coumarin derivative.

Moreover, the written description requirement does not require literal support for each claim limitation. The test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to an artisan that the inventor had possession at that time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claim language. *In re Kaslow*, 707 F.2d 1366, 1375 (Fed. Cir. 1983). Thus, a skilled artisan would have known that the Applicants were in possession of the claimed invention at the time of filing this application. Accordingly, Applicants respectfully request withdrawal of this rejection.

Additionally, claims 14-17 have been rejected as failing to comply with the written description requirement. In an effort to advance prosecution of this application and not in acquiescence of the rejection, claims 14-17 have been canceled. Accordingly, this rejection is moot.

*Discussion of Rejection Under 35 U.S.C. § 102(b)*

Claims 1, 3, and 5-15 have been rejected as allegedly anticipated by Eder et al. as evidenced by Marcu et al. Claims 14 and 15 have been canceled, and accordingly, Applicants' response will be limited to claims 1, 3 and 5-13. In support of this rejection, the

Office contends that use of the transitional phrase "consisting essentially of" in the instant claims should be construed as equivalent to the phrase "comprising" since the novel characteristics of the invention cannot be ascertained. Applicants contend that the Office has misinterpreted the phrase "consisting essentially of" in the pending claims and has unduly broadened the claims beyond the scope intended to be claimed by Applicants. The phrase "consisting essentially of" signals that the invention must include the recited steps and is only open to un-recited steps that do not materially affect the basic and novel properties of the invention. *PPG Indus. V. Guardian Indus. Corp.*, 145 F.3d 1351 (Fed. Cir. 1998). Moreover, Applicants have described above the novel characteristics of the inventive methods in view of the combination of limitations recited in the subject claims. Thus, Applicants assert that construction of the transitional phrase "consisting essentially of" to mean "comprising" is improper.

Eder et al. discloses a method of administering novobiocin in conjunction with another biologically active compound. Specifically, Eder et al. is directed to the combinatorial treatment of novobiocin and alkylating agents to mice implanted with subcutaneous fibrosarcoma. The administration of a second compound (other than novobiocin), as described in Eder et al., materially affects the basic and novel properties of the instant invention and refutes the very inference of anticipation made by the Office since it cannot be shown that by following Eder et al. that the additional compound-alkylating agent is not responsible at least in part for affecting or even killing the tumor. Specifically, the alkylating agents in conjunction with novobiocin may be the cause of tumor killing. Furthermore, the Office contends that although Eder et al. does not describe the administration of a coumarin or coumarin derivative for "about 5" days, Eder et al. discloses a 10 day treatment beginning on the sixth day post tumor implantation and the term "about" allows for the 10 day treatment to anticipate the limitation of "about 5 days." As described above, the term "about" has been held to be clear, but flexible, without materially altering the substance of the invention. A 100% increase in the number of days of administration, as the Office postulates, is more than mere flexibility in construction of the term "about" and materially alters the scope of the invention, which calls for the administration for about 5 days. Insomuch, as Eder et al. does not disclose, nor does Marcu et al. evidence, a method consisting essentially of administering about 100 mg/kg of coumarin or coumarin derivative to a mammal at least once per day for about 5 days, claim 1 is patentable over the prior art. Further, Claims 3, and 5-13 depend from claim 1 and, accordingly, Applicants respectfully request that the rejection of claims 1, 3, and 5-13 under Section 102, be withdrawn.

*Discussion of Rejection Under 35 U.S.C. § 103(a)*

Claims 1, 16, and 17 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Civitico et al. as evidenced by Hu et al. Claims 16 and 17 have been canceled, and accordingly, Applicants' response will be limited to claim 1. Applicants note that the Office bears the initial burden of factually supporting any *prima facie* conclusion of obviousness. The appropriate test to establish a *prima facie* case of obviousness demands that the Office satisfy three requirements: (1) the Office must identify some suggestion or motivation, either in the references relied upon or in the knowledge generally available in the art, to modify the references in such a way as to arrive at the invention claimed, (2) there must be a reasonable expectation of success, and (3) the prior art references relied upon must teach or suggest all of the elements of the claim. *See In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974). The Office has not met its burden in establishing a prima facie case of obviousness.

Civitico et al. teaches the ability of novobiocin to alter, *in vitro*, the pattern of viral DNA replication of duck hepatitis B virus. Civitico et al. does not teach, suggest or motivate one of ordinary skill in the art to contact a chaperone protein with a coumarin or coumarin derivative, wherein about 100 mg/kg of coumarin or coumarin derivative is administered to a mammal at least once per day for about 5 days and, wherein the chaperone protein is heat shock protein (Hsp) 90. The Office acknowledges as much; "Civitico et al. does not teach the administration of novobiocin to a mammal." Page 11. Thus, Civitico et al. do not teach, suggest or motivate a skilled artisan to reach each and every limitation of the claimed invention.

Hu et al. teaches that Hsp90 interacts with hepatitis B virus reverse transcriptase to facilitate the replication required for viral assembly and initiation of DNA synthesis. Hu et al. does not cure the deficiencies of Civitico et al. Neither Civitico et al. alone or viewed in combination with Hu et al. teach or suggest the administration of a coumarin or coumarin derivative to a mammal, wherein about 100 mg/kg of coumarin or coumarin derivative is administered at least once per day for about 5 days. Therefore, the subject matter of claim 1 would not have been obvious in view of the cited art. Accordingly, Applicants respectfully request that the rejection of claim 1 under Section 103, be withdrawn.

Claims 1, 3, and 4 are rejected under 35 U.S.C. §102(b) as being anticipated by Eder et al., as evidenced by Marcu et al., in view of Gormley et al. Applicants believe that this rejection has been marked in error as a rejection under Section 102(b) and should be responded to as a rejection under Section 103(a) in view of the Office's reliance on multiple references as a basis of this rejection. Applicants traverse this rejection.

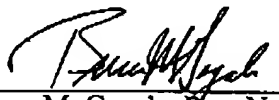
As pointed out above, Eder et al. does not teach or suggest each and every limitation of the instant claims, particularly insofar as it calls for the combinatorial administration of a

coumarin derivative with an alkylating agent. The Office does not point to a single teaching or motivation in the cited art to reach the claimed invention. Nor do the prior art references relied upon teach or suggest all of the elements of the subject claims. Marcu et al. is not prior art to this application and therefore cannot form the basis of an obviousness rejection. Gormley et al. teaches that the ATP-binding site of DNA gyrase B protein is the binding site for coumarin and coumarin derivatives, wherein such derivatives comprise chlorobiocin or coumermycin A1 and novobiocin. Gormley et al. simply teaches a different coumarin derivative not disclosed in Eder et al., but does not cure the deficiencies of Eder at al., namely the administration of a coumarin derivative independent of a bioactive alkylating agent. Thus, when viewed alone or in combination with Gormely et al., Eder at al. does not render obvious claims 1, 3, and 4 of the instant application. Accordingly, Applicants respectfully request that the rejection of claims 1, 3, and 4 under Section 103, be withdrawn.

*Conclusion*

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



Bruce M. Gagala, Reg. No. 28,844
LEYDIG, VOIT & MAYER, LTD.
Two Prudential Plaza, Suite 4900
180 North Stetson Avenue
Chicago, Illinois 60601-6780
(312) 616-5600 (telephone)
(312) 616-5700 (facsimile)

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